

Study of protein metabolism associated with diabetes mellitus

Kamalakar Mane^{1*}, Shilpa Asegaonkar², Arvind Gaikwad³, Mahendra Kamble⁴

^{1,4}Assistant Professor, ^{2,3}Associate Professor, Department of Biochemistry, Government Medical College and Cancer Hospital, Aurangabad, Maharashtra, INDIA.

Email: drkamlakarmane@gmail.com

Abstract

Background: Diabetes mellitus (DM) is a metabolic disease affecting mainly carbohydrate metabolism. Consequently, the lipid and protein metabolism area is affected. It is proposed that DM, which is due to insulin deficiency, affects protein metabolism by increasing the circulating amino acids due to decreased uptake of amino acids by the tissues. The study intends to understand the role of proteins and serum enzymes in patients of DM. **Methods:** Present study involved 100 participants of which 50 were freshly detected diabetic patients and 50 were age and sex-matched healthy controls that fulfilled inclusion criteria. Blood samples were drawn under aseptic precaution from cases of DM and healthy controls. Necessary investigations were carried out and values were tabulated for cases and controls separately for statistical evaluation. **Results:** Serum amino acid levels increased significantly ($p < 0.001$) from 8.12 (baseline) to 12.23. Glycated hemoglobin levels increased significantly ($p < 0.001$) from 5.12 (baseline) to 11.03. Total protein levels slightly decreased ($P < 0.327$) from 7.52 to 5.26. Albumin levels decreased ($P < 0.039$) from 4.01 to 4.69. Globulin level increased ($P < 0.721$) from 1.44 (baseline) to 1.89. A/G ratio levels decreased ($P < 0.631$) from 2.09 (baseline) to 1.98. AST levels decreased ($p < 0.791$) from 22.17 (baseline) to 20.32 and ALT levels were also decreased ($P < 0.627$) from 24.29 (baseline) to 21.63, which showed a small effect. **Conclusion:** Freshly detected diabetic patients were associated with a statistically significant increase in circulating amino acids, which is proportional to the percentage of glycated hemoglobin and other parameters like total protein, albumin, A/G ratio, serum enzymes AST, and ALT levels showed statistically significant decreased levels. The mechanism and clinical significance of these findings are currently unknown and warrant further study.

Key Words: Diabetes mellitus, Amino acids, Glycated hemoglobin, Amino acid Pool.

*Address for Correspondence:

Dr. Kamalakar Mane, Assistant Professor, Department of Biochemistry, Government Medical College and Cancer Hospital, Aurangabad, Maharashtra, INDIA.

Email: drkamlakarmane@gmail.com

Received Date: 03/05/2017 Revised Date: 14/06/2017 Accepted Date: 10/07/2017

DOI: <https://doi.org/10.26611/1002315>

Access this article online

Quick Response Code:



Website:

www.medpulse.in

Accessed Date:
28 July 2017

INTRODUCTION

Diabetes mellitus (DM) is the most common endocrine disease in the world today. It is a major health care problem, not only in developed nations, but also in the developing nations like India. Indeed, amongst the various ethnic groups, Asian Indians seem to be at a

particularly greater risk of developing diabetes¹. WHO estimated doubling of the total number of patients between 1994 and 2010. In round figures, the total number in the world is to rise from 110 to 230 million. While in India, the estimate rise is likely to be from 17.5 to 47.0 million². In India, at present, there are 4 to 5 crore diabetics. At the end of 2004, 28.1% of elderly (>60 years) had DM³. In rural South India, 13.4% of people are supposed to have DM⁴. Concomitant with the increasing prevalence of DM, the prevalence of micro and macrovascular accidents, peripheral vascular disease like retinopathy, neuropathy, nephropathy and other complications are likely to occur in the most productive years of life, causing severe economic and social burden⁴. Diabetes mellitus is a degenerative disease, mainly affecting carbohydrate metabolism. Consequently, lipid and protein metabolism are also affected. In case of lipids, the derangement is limited to ketosis and

ketoacidosis. In case of protein metabolism, the effect is wide spread and affects all functions of the body. Insulin is a nanabolichormone; its deficiency affects overall protein biosynthesis. This aspect is reflected by changes in circulating amino acid pool and also keyenzymes of protein metabolism namely As partateamino transferees (AST) with E.C. and Alanmine aminotransferase (ALT) with E.C. 2.6.1.2. Ageing which is a natural degenerative process also affects protein metabolism. Age in associated with diabetes mellitus will lead to increased change sinmetabolism of proteins. Hence it is proposed to study age dependent changes in aminoacidpool, serumproteins, glycated protein and transaminases. This will be correlated with changes india betesmellitus with respective age group.

AIMS and OBJECTIVES

To investigate metabolic changes in Diabetesmellitus, following parameters were studied in blood.

1. To estimate blood sugar level
2. To estimate alpha amino nitrogen inserum(amino acid pool)
3. To evaluate the activities of serum enzymes
4. AST
5. ALT
6. To estimate Serumproteins /A: G
7. To estimate Glycatedheamoglobin

MATERIAL AND METHODS

Study included 50 clinically diagnosed case of diabetesmellitus irrespective of age and sex who admitted to the Government Medical College, Aurangabad and 50 normal controls not having DM.

Method of collection

Laboratory investigation sin diabetes mellitus

Blood sugar estimation, oral glucose to larence test and urinary sugars were used for diagnosis and monitoring of diabetic patients. In addition sample were analysed for the study of glycated hemoglobin, serumenzymes, total proteins, amino acid pool. 10 ml of blood was drawn from clinically diagnosed cases of DM under asepticprecautionusing15 mldisposable syringe after taking written consent.³ separate test tubes were taken and labeled themas^{1,2,3}. Test tubelwas utilized for the estimation of blood glucose where in 2ml of blood was mixed with anticoagulant which was done by glucose oxidation method. Test tube 2 was utilized for them measurement of total proteins, AST, ALT, albuminin which 3ml of blood with noanti-coagulant that was allowed to clot and serum was separated. Test tube 3 was utilized for the estimation of glycosylated haemoglobin in which 1ml of whole blood was taken for affinity

chromatography. Blood Glucose levels were assessed by Trinder’s method, total protein levels were assessed by Biuret method. Albumin was assessed by Bromo Cresol Green Dye (BCG) method. Alanineamino transferase or SGPT was measured by IFCC (International Federation of Clinical Chemist) kinetic method. AST or SGOT was measured by IFCC kinetic method. Estimation of aminoacid nitrogen was done by method of Goodwin.

RESULTS

A Comparative study with 50 subjects in non-diabetic controls and 50 subjects in freshly detected diabetics is undertaken to study the sugar levels in non-diabetic controls and freshly detected diabetic.

Table 3: Levels of study parameters in Control and Freshly detected diabetics

Parameters	Controls		Cases		P value
	mean	SD	mean	SD	
FBS(mg/dl)	95.36	10.2	182.21	28.13	<0.001
PPBS(mg/dl)	133.14	18.01	214.4	38.17	<0.001
HbA1c %	5.12	0.49	11.03	3.7	<0.001
AAPool(mg/dl)	8.12	2.9	12.23	1.22	<0.001
Totalprotein(gm/dl)	7.52	0.48	5.26	0.78	<0.327
Albumin(gm/dl)	4.12	1.03	4.69	0.42	<0.039
Globulin(gm/dl)	1.44	1.2	1.89	0.52	<0.721
A/Gratio	2.09	0.32	1.98	0.45	<0.631
AST(IU/L)	22.17	4.27	20.32	5.12	<0.791
ALT(IU/L)	24.29	8.02	21.63	4.02	<0.627

DISCUSSION

Diabetes mellitus is the most common metabolicdisease affecting mainly carbohydrate, lipid and protein metabolism. Diabetes mellitusis mainly due to insulin deficiency or insulin resistance. Insulin beings sanabolichormoneits deficiency cause shyperglyc emia due to increased gluconeogenesis and glycogenolys is and it affects lipid and protein metabolism by causing increased lipolys is which leads to ketosis and ketoacidosis and it affects overall protein biosyn thesis which causes increased circulating amino acid pool. In our study we took 17cases of freshly detect diabetic patients and 17 cases of age and sex matched healthy controls. Freshly detected diabetics were chosen because as the study parameters will not be altered due to the rapeuticinter venations.

Blood glucose

Insulin plays a central role in regulating blood glucose (H). Deficiency of insulin or resistance to the action of insulin as seen in the diabetesme llitusis characterized by hyperglycemia. According to WHO criteria FBS126mg/dlon2 occasionsis diagnostic of diabetes mellitus (teitz). Randombloodglucose200mg/dlon2 occasionsis also diagnostic of diabetes mellitus.

In our study theme an FBS values of the patients was 182.21mg/dl diagnostic of diabetes mellitus and the PPBS was 214.4mg/dl which is high erthanupperlimitcut of f value of 140mg/dl where as control group had blood glucose values as 95.36 and 133.14 for FBS and PPBS respectively suggestive normal glycemia. These values correlate well with clinical diagnosis.

Glycated haemoglobin

Measurement of HbA1c is done to monitor or the control of blood glucose in diabetes mellitus. Alteration in blood glucose occurs from day to day depending on the dietary intake. The Glycated haemoglobin values give the average blood glucose level of preceding 2-3 months. Various studies have shown that amount of glucose attached to HbA1c increases with the duration of DM. Meena Verma and *et al*, in the study showed within the duration of diabetes mellitus, the HbA1c value also increased indicating increased insulin resistance. In another study done on Libyan women, it was found that there was a significant correlation between HbA1c and duration of DM. In our study theme an Glycated haemoglobin level of patients was 11.03% in comparison to the controls with mean of 5.12. In study done by Krolewski AS, *et al*, it was shown that the risk of microalbuminuria in patients with IDDM increased abruptly with Glycated haemoglobin above 8.1%.

Amino Acid Pool And Serum Proteins

Many studies have reported that insulin plays a key role in maintaining the amino acid level in blood in addition to its role in regulating break down and synthesis of many proteins. Insulin may enhance the synthesis rate of proteins by increasing translation of mRNA as well as increasing the gene transcription. In patients with type 1 DM, withdrawal of insulin treatment results in increased urinary nitrogen loss and in increasing circulating amino acid level. The circulating levels of branched chain amino acids (valine, leucine, isoleucine) increase in DM. The observed effects of insulin deficiency in diabetic patients vary in different body compartments, most of the effects of insulin on protein synthesis appear to occur in non-muscular tissue especially in the splanchnic area. In addition, insulin has a differential effect on hepatic protein synthesis. It inhibits fibrinogen synthesis and promotes albumin synthesis. Insulin's anabolic effect in IDDM patients is largely due to inhibition of protein breakdown. In patients with NIDDM, these effects are not noted because of residual endogenous insulin secretion. Diabetes mellitus is thus characterized by accelerated protein catabolism and amino acid catabolism which is exaggerated in the fasting state as reflected by increased uptake of alanine by the liver for gluconeogenesis and accelerated branched chain amino acid catabolism in muscles. Protein feeding also exaggerates the hyperglycemia of DM by causing

increased hepatic glucose production. In our study the mean amino acid level in patients is 12.23, mean total protein values are 5.26, mean albumin is 4.69 and mean globulin level of patients is 1.89. There is an increase in amino acid level and decrease in A/G ratio thus affecting protein metabolism.

Altered Enzymes

Due to metabolic derangements in DM, the level of serum enzymes of protein metabolism is affected. The enzymes mainly AST and ALT were elevated indirectly due to either acute tissue damage or caused due to metabolic complication of DM. It is usually seen in the post-ketotic period. Francesco Bertone, Luigi Lovuchio and Elena Nepoli studied several serum enzymes in DM; they showed that AST and ALT enzymes were elevated indirectly. In another study by Goldberg *et al*, it was shown that 17% of these patients had increased ALP activity, 15% had raised AST activity and 12% had increased LDH activity.

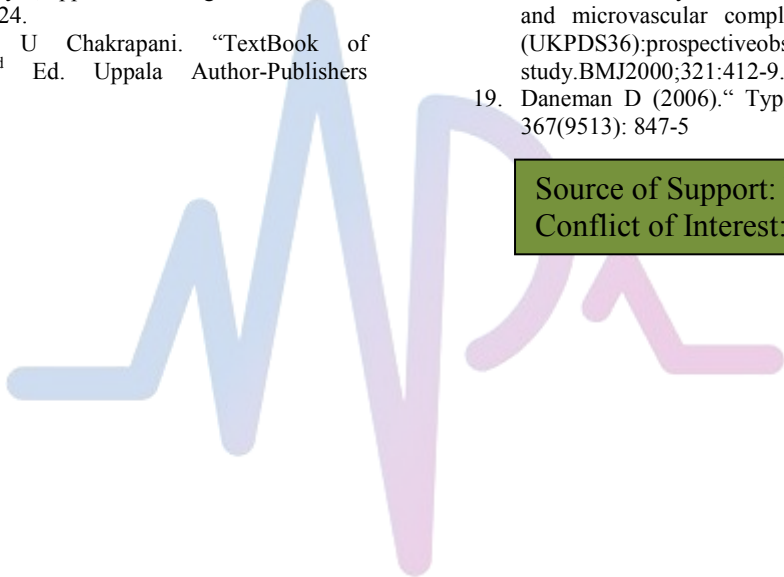
CONCLUSION

Diabetes mellitus is a degenerative disease affecting carbohydrate metabolism consequent to which lipid and protein metabolism are also affected. In DM due to insulin deficiency overall body protein synthesis is affected, which is reflected in the concentration of amino acids in the circulating amino acid pool. These changes are more pronounced with advance in age. It was observed that in DM, the circulating amino acid content increases compared to normal patients. This is proportional to the increase in percentage of Glycated Hb and other parameters like T_p, Albumin, A/G ratio and serum enzymes AST, ALT showed decrease level. Freshly detected DM is associated with statistically significant increase in amino acid pool and Glycated haemoglobin and decrease in parameters like Total protein, Albumin, A/G ratio and serum enzymes AST, ALT level.

REFERENCES

1. Enas. A. "prevalence of coronary artery disease in Asian Indians". American journal of cardiology, 1992; 70:945-9.
2. Biuti, B. Tripathy. Diabetes mellitus, some challenges and controversies. JIMI 1998; 9:27-9.
3. Munichudappa C. Epidemiology and burden of type 2 diabetes mellitus, Bangalore: type 2 diabetes-The Indian scenario, Ed. Jayaram BM, micro labs ltd 2002: 13
4. Dr. Ramachandran A, Snehalatha C, Kapur A, Mohan V, Vijay V, Das AK "High prevalence of DM and impaired glucose tolerance in India; National urban diabetes survey. Diabetologia 2001; 44:1094-1108.
5. Leo. P, Krall, Rachmil Levine, Donald Barneth. "The history of diabetes" Ronald Khan, Joslin's DM, 13th Ed, A Waverly Company 1994; 1-7.

6. Vasudevan D, Mand Sreekumari S, Banting FG, Best CH, Collip JB, Campbell WR, Fletcher AA (1922). "Pancreatic extracts in treatment of diabetes mellitus" *Canad Med Association J* 12:141-146.
7. Himsworth (1936). "Diabetes mellitus: its differentiation in to insulin sensitive and insulin insensitive types" *Lancet* I:127-130.
8. Yalow RS, Berson SA, (1960). "Immunoassay of endogenous plasma insulin in man". *J. Clin. Invest.* 39:1157-75
9. Dennis L Kasper, Eugene Brawnwald, Anthony SFonci, Stephen LHauser, DanL Lango, JLavyJameson, Harrison's principles of Internal medicine. 16th Ed. Mc.Graw-Hill, Medical publishing division; 2005
10. Vasudevan DM and sreekumari S "Textbook of Biochemistry for Medical students" 4th Ed Jaypee brothers Medical publishers (P) Ltd; 2005
11. Victor W. Rodwell, Robert K Murray, Daryl K Granner, chapter 12 in Harper's Biochemistry 25th Ed, Robert K, Murray, Daryl K, Granner, Peter A. Mayer, Appleton and Lange Stamford, Connecticut 2000, page 324.
12. U Satyanarayan, U Chakrapani. "Text Book of Biochemistry" 3rd Ed. Uppala Author-Publishers interlinks: 2006.
13. Robert K Murray, Daryl K Granner, Peter A Mayer, Victor M Rodwell. Harper's Illustrated Biochemistry. 26th Ed. McGraw-Hill publishers: 2003.
14. Abu-Leddeh HS, Nair KS, Mayo clinic, Rochester MN 55905, USA [PMID: 90022953 (Indexed for medline)]
15. Richard A Harvey, Pamela C Champe, Lippincott's Illustrated reviews, "Diabetes mellitus" Chapter 25, page 335, Indian Edition, 3rd Ed. Jaypee Brothers Medical publishers (P) Ltd.
16. Nathan DM, Cleasy PA, Backlund JY, et al (2005) "Intensive Diabetes Treatment and Cardiovascular disease in patients with type 1 diabetes". *N. Engl. J. Med* 353(25):2643-53. DOI: 10.1056/NEJMoa052187.
17. The Diabetes control and complication trial research group. The effect of intensive Diabetic therapy on development and progression of neuropathy. *Annual Internal Med* 1995; 122:561-8.
18. Adler AI, Stratton IM, Neil HA, Yudkin JS, Mathews DR, Cull CA, Wright AD, Turnes RL, Holman RR. Association of systolic blood pressure with microvascular and microvascular complications of type 2 diabetes (UKPDS 36): prospective observational study. *BMJ* 2000; 321:412-9.
19. Daneman D (2006). "Type 1 Diabetes mellitus" *Lancet* 367(9513): 847-5



Source of Support: None Declared
Conflict of Interest: None Declared